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Application Number	09/783,320
Filing Date	02/15/01
First Named Inventor	Walke
Group Art Unit	1652
Examiner Name	D. M. Ramirez
Attorney Docket Number	LEX-0137-USA

ENCLOSURES *(check all that apply)*

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SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Lexicon Genetics Incorporated Lance K. Ishimoto Reg. No. 41,866
Signature	Reg No 40162
Date	June 7, 2004

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant(s):	D. Wade Walke, *et al.*	Group Art Unit: 1652
Application No.:	09/783,320	Examiner: D.M. Ramirez
Filed:	02/15/01	
Title: Novel Human Kinases and Polynucleotides Encoding the Same		Atty. Docket No. LEX-0137-USA

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
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Alexandria, VA 22313-1450

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REPLY BRIEF

Sir:

Appellants hereby submit an original and two copies of this Reply Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Examiner's Answer mailed on April 6, 2004 which is due on June 6, 2004 which falls on a Sunday and is therefore extended to Monday June 7, 2004. This Reply Brief is thus timely submitted.

Appellants believe no additional fees are due in connection with this Reply Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

Appellants agree with the Examiner's assertion that "A statement identifying the real party in interest is contained in the brief" (Examiner's Answer at page 2).

II. RELATED APPEALS AND INTERFERENCES

Appellants agree with the Examiner's assertion that "Appellant's brief includes a statement that there are not related appeals or interferences." (Examiner's Answer at page 2).

III. STATUS OF THE CLAIMS

Appellants agree with the Examiner's assertion that "The statement of the status of the claims contained in the brief is correct." (Examiner's Answer at page 2).

IV. STATUS OF THE AMENDMENTS AFTER FINAL

Appellants agree with the Examiner's assertion that "Appellant's brief contains a statement indicating that there are no additional outstanding amendments." (Examiner's Answer at page 2).

V. SUMMARY OF THE INVENTION

Appellants agree with the Examiner's assertion that "The summary of invention contained in the brief is substantially correct." (Examiner's Answer at page 2).

VI. ISSUES ON APPEAL

Appellants agree with the Examiner's assertion that "The appellant's statement of the issues in the brief is correct." (Examiner's Answer at page 2).

VII. GROUPING OF THE CLAIMS

Appellants agree with the Examiner's assertion that "The brief contains a statement indicating that claims in each of the issues shall stand or fall together as a group." (Examiner's Answer at page 2).

VIII. CLAIMS APPEALED

Appellants agree with the Examiner's assertion that "The copy of the appealed claims contained in the Appendix to the brief is correct" (Examiner's Answer at page 2).

IX. PRIOR ART OF RECORD

Appellants agree substantially with the Examiner's assertion as to the art previously presented in this case (Examiner's Answer at page 2-3).

X. ARGUMENT

A. Do Claims 4, 11 and 12 Lack a Patentable Utility?

Appellants do not wish to restate all of the arguments presented in the Appeal Brief concerning the Examiner's allegation that claims 4, 11 and 12 lack a patentable utility, and instead incorporate the entirety of Section VIII(A) of the Appeal Brief at this point herein by reference. However, Appellants do feel the need to specifically address several of the arguments presented in the Examiner's Answer ("the Answer") in some detail in order to clarify the record.

The Examiner repeatedly emphasizes and states that the basis of these rejections is a complete lack of knowledge as to the "type" of protein kinase that is encoded by the sequences of the present invention and that the biological function and/or diseases/disorders is unknown (see for example, page 28, lines 1-4 and again at line 21 through page 29, line 1; page 30, lines 8-12). Appellants could not disagree more.

Appellants herein summarize their position and the supporting evidence provided in the present case. Appellants have asserted that the sequences of the present invention encode a novel human kinase protein. The function of kinase proteins is both well known and implied to those of skill in the art. Protein kinases have a well-established use in the molecular biology art based on this class of proteins ability to phosphorylate proteins at serine and threonine residues, (this utility is so well known that U.S. Patent No. 5,817,479 has issued on human kinase fragments). Evidence has been submitted (Exhibit A) that the sequences of the present invention (SEQ ID NO:4) are 96.343% identical at the amino acid level over the entire length with a human kinase protein annotated by third party scientists wholly unaffiliated with Appellants as human Nek-1. The, mouse homolog of the human kinase gene, murine Nek-1 has been "knocked out" and NEK-1 has been recognized to participate in signaling pathways that regulate cellular processes and additionally the elimination of Nek1 activity lead to a progressive polycystic kidney disease in the mice. Thus the function of Nek-1 has been established, as has the association of Nek-1 with polycystic kidney disease. The sequences of the present invention, which encodes a human homolog of the Nek-1 gene have an ascribed function and a disease association that is known to those of skill in the art. Certainly the present situation is analogous to Example 10 of the Revised Interim Utility Guidelines Training Materials. Thus, clearly the sequences of the present invention have a specific, substantial and well

recognized utility. The Examiner has chosen to discount much of the evidence provided thus far and thus it falls to the Board to resolve this issue.

Appellants would first like to resolve a repeated error on the part of the Examiners' requirements and expectations. Although the Answer repeatedly points to the lack of Appellants referral to the kinase of the present invention in the specification as NEK-1 as somehow indicating a lack of knowledge with regards to the protein, this is completely unfounded. The lack of Appellants' referral to the human protein kinase as NEK-1 reflects only Appellants inability to presage a decision that would be made at a later date by others to refer to the novel human kinase protein encoded by the sequences of the present invention as human Nek-1.

The Answer also expresses the repeated opinion that "the mouse protein of Letwin et al. (774 amino acids long), is at best 54% sequence identical to the polypeptide of SEQ ID NO:4 (665 matches; 54% =665x100/1214). See alignment." (Answer at page 8, lines 23 through page 9, line 1). First, no alignment appears to have been provided with the Answer. Second, Appellants are unsure as to the propriety of the introduction of new evidence by the Examiner in the Examiners' Answer. That said, Appellants are a little confused by the Examiner's statements for after performing their own alignment and analysis Appellants found that the alignment of the human kinase protein of SEQ ID NO:4 and the mouse protein sequence of Letwin, *et al.* is actually quite good for a cross species analysis. While the mouse sequence is described by Letwin *et al.* is shorter than the human sequence of SEQ ID NO:4, the described mouse protein sequence showed very good identity for an ortholog in another species (85.476% over the full length of the sequence of Letwin, *et al.* as represented in GenBank accession no: AAB23529, with 665 of its 744 amino acid matching). Furthermore, by overlaying the human protein onto the mouse genome (BLAT analysis) Appellants were able to establish that the downstream sequence missing from the shorter mouse protein described in Letwin, *et al.*(AAB23529) that is present in the human protein of SEQ ID NO:4 is actually present in the mouse genome and exists immediately downstream of the sequence described by Letwin, *et al.*. This provides additional evidence supporting the claimed relationship between the mouse sequence of Letwin, *et al.* and the human sequence of SEQ ID NO:4, strongly indicating that the kinase of SEQ ID NO:4 is the human homolog of the mouse kinase Nek-1 described by Letwin, *et al.*

In the absence of evidence to the contrary, these assertions which are clearly credible to those of skill in the art should direct further discussions.

As still further support for Appellants' description of the sequences of the present invention as the human homolog of the Nek-1 mouse gene is the fact that those of skill in the art, as exemplified to a high standard by those working at The National Center for Biotechology Information (NCBI), have linked the mouse protein sequence of Letwin, *et al.* to a human protein sequence, GenBank accession no: NP_036356, which is annotated by others *in no way affiliated* with Appellants as "NIMA (never in mitosis-protein kinase Nek1 [Homo sapiens]". The amino acid sequence of NP_036356 is identical to that of accession no.: Q96PY6, which was compared previously with SEQ ID NO:4 and the alignment submitted with an earlier Response and in the Appeal Brief as Exhibit A. The alignment provided in Exhibit A shows that Q96PY6 is 96.343% identical at the amino acid level over the entire length of the described sequence to a protein that has been annotated by third party scientists wholly unaffiliated with Appellants as *Homo sapiens* (Human) SERINE/THREONINE KINASE NEK-1. Clearly Appellants' assertions are credible as those of skill in the art when provided the same information came to the same conclusion. The Answer refers to this sequence as that of Nagase, *et al.* Thus clearly, the human kinase protein of SEQ ID NO:4 is the human homolog of the mouse Nek1 kinase protein, whose activity was described by Letwin, *et al.* and an isoform (96.343% identical) of the human kinase protein which others identified by others as human serine/threonine kinase Nek-1. All of which evidence is consistent with Appellants assertions that SEQ ID NO:4 encodes an isoform of human serine/threonine kinase Nek-1.

The Examiner, however, discounts this evidence and is not convinced with functional evidence provided using the mouse protein, as indicated by the emphasis on "in mice" (page 8, line 10) and by the statement "the only experimentally determined NEK-1 protein, i.e. the mouse NEK-1 protein of Letwin et al." (page 8, line 23-24). Further, on page 9, lines 9-12, the Examiner's Answer states

"Therefore, while one could reasonably conclude that a human NEK-1 protein may have a similar biological role to that characterized by Letwin et al. and Upadhya et al. in mice, in view of the uncertainty in regard to the real function of the polypeptide of SEQ ID NO:4 and the polypeptide of Nagase et al.,

and the unpredicatability of the art in regard to assigning function based solely on structural homology, it is not reasonable for one of skill in the art to conclude that Appellants polynucleotides have a specific and substantial or well-established utility "

While having accepted as reasonable Appellants' assertions that human Nek-1 protein is the human homolog of, and thus would logically share biological function with, the functionally characterized and disease associated Nek-1 of the mouse. The Examiner appears to be of the opinion that only data obtained directly in humans will be persuasive. This is clearly not the legal standard for patentable utility recognized by the U.S. Courts nor is such a requirement described in the new USPTO Utility Guidlines or the MPEP for Appellants are not aware that there is a requirement for "*in vivo*" human evidence, nor any form of "*in vivo*" evidence *per se* in the new USPTO utility guidelines or the MPEP and no U.S. case law, of which Appellants are aware, that even suggests the requirement for "*in vivo*" evidence, human or otherwise to establish patentable utility. Furthermore, such is not even the accepted scientific standard by those of skill in the art, for it negates all evidence obtained through "*in vitro*" experimentation. In light of the myriad ethical and legal issues surrounding human experimentation, those of skill in the art readily accept that the best "*in vivo*" evidence that is to be reasonably expected (prior to FDA involvement) is that obtained in experimental animal models, such as mice.

The Examiner's position that one cannot predict homologous function from homologous proteins in animals of a different species appears to be based of a few contrarian publications regarding exceptional failures of bioinformatic analysis, which do not describe the Nek-1 sequences nor even a kinase (likely because kinases domains are so well-known to the art). Interestingly this is perfectly acceptable to the Examiner, who in contrast, as described in the Answer (page 27, lines 1-7) is apparently of the opinion that the various mandatory legal precedents provided in Federal Circuit decisions are narrowly limited to the particular technologies discussed in each specific case. If this were indeed true, which is clearly not the case, the Federal Circuit's various articulations of the legal standards for utility, enablement, doctrine of equivalents, etc., for juice dispenser inventions, for example, would have virtually no bearing on similar legal inquiries relating to electrical inventions, business methods, or inventions from distinct arts. Appellants

contend that the Examiner's articulated position lacks any legal and procedural foundation and is intellectually unsound. Indeed, one might presume to speculate that a Federal Circuit panel would find the Examiner's stated position as representing a rather remarkable deviation from established legal precedent.

The Answer then goes on to describe again the contrarian article by Bork (Genome Research *10*:398-400, 2000) on which the allegation that the art recognizes that function cannot be predicted from structure alone. On this basis alone the Examiner fully disregards the scientific evidence provided by Appellants, that SEQ ID NO:4 encodes a kinase that those of skill in the art have readily recognized as an isoform of human Nek-1. Additionally, the Examiner contends that the evidence provide by Appellants in the form of the peer reviewed publications is insufficient because Nagase, *et al.*, does not provide any experimental corroboration" (Answer at page 8, line 14) and that "Nagase, *et al.*, like Appellants, assigned a putative function of the polypeptide disclosed based solely on structural homology" (Answer at page 8, lines15-17). Appellants respectfully point out that such is the standard of the scientific community (those of skill in the art) and ask if not by structural and genomic homology (as described above) how else would one establish that a protein in one species is the homolog or ortholog of a protein in another species? These methods are those that are used and accepted by those of skill in the art. As such, one would also reasonably expect that this evidence would also are acceptable to establish patentable utility.

The Examiners' opinion that structure and function have an unpredictable relationship also runs counter to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence that has a similarity score of 95% to a protein having a known function. The presently claimed full length sequence that has a similarity score of 96.343% to a protein having a known function (Nek-1).

The Answer reiterates the Examiner's previous opinion, disregarding the above, the and details the few, dated and largely irrelevant examples that were submitted in support of its untenable position a that structural homology is not sufficient to assign function. The Examiner's Answer again describes Bork (Genome Research *10*:398-400, 2000) as supporting the proposition that prediction of protein function

from homology information is somewhat unpredictable. The Answer directs attention to page 399, on which the author notes the limitations of various methods of analysis. It is of interest that in his "analysis" Bork often uses citations to many of his own previous publications, an interesting approach. ' My position is supported by my previous disclosures of my position.' If Bork's position is supported by others of skill in the art, one would expect that he would reference them rather than himself to provide support for his statements. Given that the standard with regard to obtaining U.S. patents is those of skill in the art, this observation casts doubt on the broad applicability of Bork's position. It should also be noted that in Table 1, on page 399, in which selected examples of prediction accuracy are presented, that the reported accuracy of the methods which Appellants have employed are, in fact, very high. While nowhere in Bork is there a comparison of the prediction accuracy based on the percentage homology between two proteins or two classes of proteins, " Homology (several methods)" is assigned an accuracy rate of 98% and "Functional features by homology" is assigned an accuracy rate of 90%. Given that these figures were obtained based on what is at least a 4 year old analysis, these high levels of accuracy would appear to support rather than refute Appellants assertions in the present case. Additionally Bork even states (on page 400, second column, line 17) that " However, there is still no doubt that sequence analysis is extremely powerful". In summary, it is clear that it is not Bork's intention to refute the value of sequence analysis but rather he is indicating that there is room for improvement .

The Answer also reiterates its position with Broun *et al.* (Science *282*:1315-1317, 1998), Van de Loo *et al.* (Proc. Natl. Acad. Sci. USA *92*:6743-6747, 1995), Seffernick *et al.*, (J. Bacterol; 183(8):2405-2410, 2001) and Witkowski, *et al.*, (Biochemisty 38:11643-11650, 1999) as teaching that prediction of function based on homology is unpredictable. However, each of these papers cite only single rare examples, where function based on sequence homology, had it occurred, might have been proven to be incorrect. These papers do not refer to Nek-1 nor, as the Answer concedes (page 12, line 5), do they even refer to a kinase protein, likely because kinase proteins are well-known to contain established active domains.

Appellants point out that a careful reading of the "relevant literature" submitted by the Examiner does not support the concept that function cannot be based on sequence and structural similarity, in contrast

many of the examples actually support the use of such methodologies while identifying several areas in which caution should be exercised. As stated previously these inaccuracies and potential pitfalls can be overcome by a more careful analysis by those of skill in the art. Automatic methods of sequence homology identification was only the staring point for consideration the sequences of the present invention underwent careful analysis by a series of individuals of skill in the art, many highly qualified (B.S. and Ph.D. level scientists).

Furthermore, these articles are just examples of the few contrarian articles that the PTO has repeatedly attempted to use to deny the utility of nucleic acid sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions. While there may not be a 100% consensus within the scientific community regarding prediction of protein function from homology information this is not unusual, in the scientific community or the legal community, nor is it indicative of a general lack of consensus. A few rare exceptions do not a rule make.

Further supporting the position that bioinformatic information is recognized to be of value by those of skill in the art is the result of a recent search of the NCBI-NLM-NIH public scientific database "PubMed" using the term "bioinformatics" which resulted in 5,548 different scientific publications (these will not be provided to avoid burdening the USPTO's scanning group). If bioinformatic information is not a method accepted by those of skill in the art to predict protein function based on structural information, why are so many publications reporting the results of its use? Clearly this suggest that the vast majority of those of skill in the art do recognize a structure- function relationship and view bioinformatic information as both useful and valid.

Another form of evidence supporting the position that bioinformatic information is recognized to be of value by those of skill in the art is the fact that many scientists, corporations and institutions elect to allocate significant proportions of their limited resources for access to private bioinformatic systems and databases. Thus, it would appear obvious that the majority of those of skill in the art value such structural based analyses and accept the findings of bioinformatic analysis for they are willing to pay dearly for access to such information.

Still another and perhaps most persuasive, form of evidence supporting the position that bioinformatic information is recognized to be of value by those of skill in the art is the issuance of multiple U.S. patents regarding bioinformatic prediction and methods for doing the same (see for example, U.S. Patent Nos. 6,229,911, 6,466,874, 6,567,540, 6,615,141, 6,631,331, 6,651,008, 6,677,114, copies of these patents are not provided pursuant to current Office policy). Of particular interest might be U.S. Patent No. 6,466,874, one of whose claims reads on "A method of identifying proteins as functionally linked, the method comprising comparing sequences to find homologous functional domains." As issued U.S. patents are legally presumed to be valid, one must presume that the method of carrying out an analysis based on structure-function relationship has utility. One must logically, therefore, presume that both those of skill in the art and the USPTO recognize the utility of structural homology based bioinformatic prediction.

Appellants respectfully point out that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be believable. Appellants submit that the overwhelming majority of those of skill in the relevant art would believe prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by extensive number of journal articles (which support Appellants' assertion that the overwhelming majority of those of skill in the art place a high value on prediction of protein function from homology information and the usefulness of bioinformatic predictions), and would thus believe that Appellants' sequence is a human kinase protein, (NEK-1) whose function has been described. As believability is the standard for meeting the utility requirement of 35 U.S.C. § 101, Appellants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101.

Appellants also note that even the USPTO itself does not require 100% identity between proteins to establish functional homology. The Examiner's position that homology of SEQ ID NO:4 to a known protein with a known function does not endow SEQ ID NO:4 with the function is contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently

claimed sequence) that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA. .....Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

In the present case it is clear that the sequences of the present invention encode a novel human serine/threonine protein kinase. In contrast to the Examiner's position, those of skill in the art recognize that serine/threonine protein kinases have a well-established use in the molecular biology art based on this class of proteins ability to phosphorylate proteins at serine and threonine residues. The utility of protein kinases is so well-established that U.S. patents frequently issue (see for example, Appellants own recently issued patents) on kinase proteins and U.S. Patent No. 5,817,479 has issued on human kinase fragments (copies of issued patents are not provided pursuant to current Office policy). Again, as issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see below). Appellants therefore respectfully submit that if fragments of a human kinase protein have utility, then surely the present sequences that encode an entire full-length human kinase protein that is known to the art as Nek-1 must also meet the requirements of 35 U.S.C. § 101 and the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should be overturned.

Clearly the specific scientific evidence submitted supports Appellants' assertions that the sequences of the present invention encode a novel human kinase protein (specifically NEK-1), a class of proteins for which there is a well established utility that is recognized by those of skill in the art. Further, the specific biological function of Nek-1 kinase in the mouse has been established, thus those of skill in the art would recognize the specific and substantial utility of a novel isoform of human Nek-1. Therefore, according to the guidelines "Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed...Thus the conclusion reached from this analysis

is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made." Thus the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should be overturned.

Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101 and note that if an issued U.S. patent were to be considered to be invalid by the USPTO, one would anticipate that Patent to be a candidate for *ex parte* reexamination procedures.

According to the guidelines "Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed...Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made." Thus the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should be overturned.

In the Answer, t he Examiner appears to be confusing several issues in stating, for example on page 22, line 5, the Examiner states "The specification provides no information or guidance as to the specific biological function and/or disease associated with changes in expression patterns or the detection/identification of transcripts." Appellants respectfully submit that had Appellants claimed a method of using the sequences of the present invention in a gene chip to differentiate those with and without polycystic kidney disease (for example), then clearly the specification would have to disclose the detailed information the Examiner is requiring simply to establish patentable utility. However Appellants have not claimed any specific methods of use rather they have claimed a specific composition of matter. And have provided these methods of use to exemplify the multitude of utilities that those of skill in the art would recognize the utility of the claimed invention.

The Answer also, at page 24, lines 10- 11 emphasizes that "the specification does not provide any information as to the actual genomic locus (i.e.: chromosomal position of the gene) which corresponds to the claimed polynucleotides." Again had Appellants claimed a method of using the sequences of the present

invention to identify a genomic locus then clearly the specification would have to disclose the detailed information the Examiner is requiring simply to establish utility. However, Appellants have not claimed a method of using the sequences of the present invention to identify a genomic locus, rather they have claimed a specific composition of matter. And have provided these methods of use to exemplify the multitude of utilities that those of skill in the art would recognize for the composition. Additionally, given the inability of the Examiner to readily see the ease with which those of skill in the art can use the sequences of the present invention to map the genome, Appellants provided evidence obtained within minutes using only the information provided in the specification and the ability to overlay these specific sequences to the known human genome, results shown in Exhibit L, and thus obtained the "actual genomic locus" (4q32.3) which is the same position to which the human kinase called NEK-1 has been mapped by others of skill in the art. Evidence has thus been provided that demonstrates that the asserted utility was credible and that clearly those of skill in the art find the asserted utility to be credible as they have used it to as asserted to map this human kinase to a specific position in the human chromosome.

The Examiner discounts several arguments concerning the utilities of the sequences of the present invention since other nucleic acid sequences can be used in a similar fashion. In addition to the detailed arguments presented by Appellants in the Appeal Brief with regard to each of these asserted utilities, Appellants once again point out that these arguments are completely rebuffed by the Federal Circuit's holding in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "[A]n invention need not be the best or only way to accomplish a certain result"). As the main argument concerning this utility and that of use of the specific sequences on DNA chips (presented below) is that since other nucleic acid sequences can be used to map the human chromosome or on DNA chips, these do not represent specific or substantial utilities. However, as previously presented, don't all golf balls and tires have the same utility of other golf balls or tires, i.e. they can be used as golf balls or tires respectively and yet these items are readily considered to have patentable utility.

Furthermore, it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re*

Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Appellants respectfully point out that knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. In fact some such gene chips have contained randomly generated sequence.

However, in contrast the sequences of the present invention provide a specific marker of the gene that is transcribed, spliced and encodes a novel human transporter that is expressed in some human tissues and not others. Thus, these sequences provide a unique identifier of the corresponding gene in the human genome. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. The Examiner agrees that such "DNA chips" have utility, as evidenced by hundreds of issued U.S. Patents, but argues that specific sequences which clearly increase the utility of a patented invention do not. It must be noted that this position runs counter to that made by the Examiner regarding golf balls, wherein the presence of a specific feature that enhances the utility of the golf ball has utility.

Additionally, as discussed briefly above the Examiner is apparently of the opinion that the various mandatory legal precedents provided in Federal Circuit decisions are narrowly limited to the particular technologies discussed in each specific case (see page 27, lines1-7). If this were indeed true, which is clearly not the case, the Federal Circuit's various articulations of the legal standards for utility, enablement, doctrine of equivalents, etc., for juice dispenser inventions, for example, would have virtually no bearing

on similar legal inquiries relating to electrical inventions, business methods, or inventions from distinct arts. Appellants again contend that the Examiner's articulated position lacks any legal and procedural foundation and is intellectually unsound. Indeed, one might presume to speculate that a Federal Circuit panel would find the Examiner's stated position as representing a rather remarkable deviation from established legal precedent.

Finally, while accepting the Examiner's right to withhold comment and with full recognition of the fact that all patent applications are examined on their own merits and that the prosecution of one patent does not effect the prosecution of another patent, *In re Wertheim,* 541 F.2d 257, 264, 191 USPQ 90, 97 (CCPA 1976), however the issue at hand in one of whether the fact that patents issue regularly that have issued recognizing the utility of a class of molecules does this confers a statutory precedent of patentability to a broad class of compositions (kinase proteins). Thus, there remains a lingering issue regarding due process and equitable treatment under the law. While Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, Appellants respectfully submit that it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. Given the rapid pace of development in the biotechnology arts, it is difficult for the Appellants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than prior inventions that were issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, it stands to reason that Appellants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record in the Appeal Brief. Thus, holding Appellants invention to a different standard of utility appears inconsistent and inequitable, such a judgement being arbitrary and capricious, a violation of due process and equal protection under the

law.

In summary, in the present case Appellants asserted that the sequences of the present invention encode a novel human kinase protein in the specification as filed. The function of kinase proteins is both well known and implied to those of skill in the art and protein kinases have a well-established use in the molecular biology art based on this class of proteins ability to phosphorylate proteins at serine and threonine residues. Appellants have established, through several forms of evidence, that those of skill in the art recognize the sequences of the present invention as encoding an isoform of the human kinase protein Nek-1. In mice, the biological function and a disease association has been established for the mouse homolog of the human kinase Nek-1. Thus, in addition to the well-established and well-recognized utilities for protein kinases, the sequences of the present invention which encode an isoform of human kinase Nek-1 has an established biological function known to those of skill in the art and a disease association that is also recognized by those of skill in the art. Therefore, certainly the present situation is analogous to Example 10 of the Revised Interim Utility Guidelines Training Materials. Thus, clearly the sequences of the present invention have a specific, substantial and well recognized utility.

In view of the overwhelming evidence of the substantial, credible, specific, and well-established utility of the presently claimed invention, and in view of the absence of any evidence of record specifically refuting the utility of the human kinase protein encoded by the sequences of the present invention, the Appellants' respectfully request that the Board overrule the pending rejection of claims 4, 11 and 12 under 35 U.S.C. section 101 as well as the related rejections under 35 U.S.C. section 112, first paragraph.

B. Are Claims 4, 11 and 12 and 14 Unusable Due to a Lack of Patentable Utility?

Regarding the rejection of claims 4, 11 and 12 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility, Appellants submit that as claims 4, 11 and 12 have been shown to have "a specific, substantial, and credible utility", as detailed in previous Responses, Section X(A) above, as well as Section VIII(A) of the Appeal Brief, the present rejection of claims 4, 11 and 12 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore respectfully submit that the rejection of claims 4, 11 and 12 under 35 U.S.C. § 112, first paragraph, should be overruled.

XI. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 4, 11 and 12 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overrule the Final Action's rejections.

Respectfully submitted,

June 7, 2004
Date

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